REMARKS

Allowable Subject Matter

In the May 17, 2004 Office Action, Examiner Winkler found claims 2-4 and 55 allowable. In light of the allowability of claims 2-4, applicants have amended claims 10-12 to depend from allowable claim 4, and as such, should be found to be allowable. Claims 13-16 as previously presented already depended from allowable claims 2-4, and as such, are also allowable. Applicants have added new product claims 58-63 that depend from claim 4 that are comparable to allowed claim 55, and thus, meet all the requirements of patentability.

Rejoinder of Method Claims

When an application as originally filed discloses a product and the process for making and/or using such product, and only the claims directed to the product are presented for examination, when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product for examination through rejoinder procedure in accordance with MPEP §821.04, provided that the process claims depend from or include all the limitations of the allowed product claims.

Applicants have consistently amended the method claims during the prosecution of this application with the intent to rejoin the withdrawn method claims when the product claims were determined to be allowable. Thus, the currently pending method claims include all the limitations of the allowed product claims and meet all standards of enablement, written description and definiteness under 35 U.S.C. §112. Method claim 39 and claims depending therefrom recite a method to induce an immune response, wherein the immune response comprises the production of antibodies after administration of the chimeric polypeptides of claim 4. Support for this method may be found in Example XI. Independent method claims 45 and 49 and claims depending therefrom recite methods to identifying an agent that inhibits an interaction between the HIV virus and a virus receptor or virus-coreceptor. Support for these method claims can be located in Examples IV, VI, IX and X. New method claims 64-69 depend from allowable product claims and recite methods described hereinabove.

Accordingly, the method claims are in form suitable for future examination upon their rejoinder with the allowed product elected claims. Applicants are requesting that method claims 39, 41-45, 47-50 and 64-69 be rejoined, examined and found allowable.

Rejections of Claims and Traversal Thereof

In the May 17, 2004 Office Action,

claims 1, 5-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Young, et al. (U.S. Patent No. 6,060,316, hereinafter Young) and DeVico, et al (U.S. Patent No. 5,843,454, hereinafter DeVico '454) or DeVico, et al. (U.S. Patent No. 5,518,723, hereinafter DeVico '723) in view of Freed et al. Journal of Virology 1989, in further view of Stratagene Catalog (1997/1998);

claims 1, 5-11 and 15-16 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of DeVico '723 or claim 1 of DeVico '454 in view of Young and Freed.

The above-defined rejections of claims 1 and 5-16 are hereby traversed.

Rejection under 35 U.S.C. §103(a)

Claims 1, 5-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Young and DeVico '454 or DeVico'723 in view of Freed and in further view of Stratagene Catalog. Applicants submit that the combination of the cited references does not in any way render applicants' claimed invention *prima facie* obvious.

The present invention relates to a chimeric polypeptide comprising: a HIV virus coat polypeptide sequence and a viral receptor polypeptide sequence, wherein the HIV virus coat polypeptide sequence has a bonding affinity for the viral receptor polypeptide sequence, wherein the HIV virus coat polypeptide sequence and the viral receptor polypeptide sequence are linked by an amino acid spacer of sufficient length to allow the HIV virus coat polypeptide sequence and the viral receptor polypeptide sequence to bind to each other, and wherein the HIV virus coat polypeptide is gp120 comprising a mutated furin cleavage site on the C-terminus of gp120.

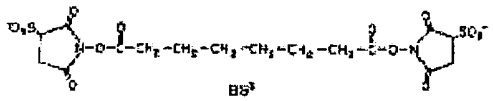
The Young reference describes a method of infecting a cell with a viral vector. To activate the viral entry of the viral vector, a soluble viral receptor-ligand fusion molecule is added. The soluble viral receptor-ligand fusion molecule comprises a viral receptor moiety that binds to the envelope component

of the viral vector and a ligand moiety that binds to a cell-type specific cellular receptor. An amino acid linker may be positioned between the viral receptor moiety and the ligand moiety and is of sufficient length to separate the moieties in space, thereby not restricting the ability of the soluble viral receptor-ligand fusion molecule to bind independently and maintain the proper conformation, as stated at column 10, lines 1-5 of Young.

DeVico '454 and DeVico '723 disclose a gp120-CD4 covalently bonded complex that is chemically bonded together with a crosslinking agent. Thus, the virus coat polypeptide sequence and the receptor polypeptide sequence are two separate components that are **chemically cross-linked to form a receptor-ligand complex.** Both DeVico '454 and DeVico '723 expressly state that:

> "We used a covalently linked gp120-CD4 complex as an immunogen. gp120 molecules were covalently coupled to soluble recombinant CD4 using **bivalent cross-linking agents** to ensure that the integrity of the complexes was maintained during any manipulations." (emphasis added) (see column 4, lines 47-51; column 4, lines 17-21; respectively)

Furthermore, as described in the examples set forth in DeVico '454 and DeVico '723, steps were taken to permanently bond the virus coat polypeptide and viral receptor polypeptide with a bivalent cross-linking agent that covalently linked them together. Bis-sulfosuccinimidyl suberate was the crosslinking agent used in Examples I, II and III, which is a homobifunctional cross-linking reagent with amine reactivity having a structure as set forth below:



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This crosslinking agent forms a complex that is not a single chain polypeptide wherein the amino acid spacer forms peptide bonds between the terminal α-amino group of one protein and the terminal α-carboxyl group of protein. Instead the crosslinking agent binds only to primary amines on the respective proteins, and as such, the formed complex is entirely different from the chimeras of the presently claimed invention because the end product is not a polypeptide chain.

DeVico '454 and DeVico '723 expressly state that the use of the covalently bonded complex is important because prior art complexes formed through natural affinity (formed by natural attraction of receptor and

ligand) did not provide for the antibodies raised strictly for the complex and instead reacted with gp 120 or CD4 (See column 2, lines 42-49; column 2, lines 41-44; respectively).

Clearly, DeVico '454 and DeVico '723 disclose only covalently bonded complexes and do not disclose, teach or suggest a chimeric polypeptide that is a linear polypeptide chain comprising a virus coat polypeptide sequence and a receptor polypeptide sequence linked by an amino acid sequence spacer therebetween.

According to the Office:

> "It would be obvious to one of ordinary skill in the art at the time the invention was made to utilize a chimera for the production of the gp120-CD4 complex. . . . The addition of amino acid linkers would have been obvious to the ordinary artisan in order to alleviate potential folding constraints in the fusion protein as suggested by Young, et al.(see column 10, lines 1-5)."

Applicants vigorously disagree.

In order to determine obviousness, it is incumbent upon the Office to view the invention as a whole. *In re Wesslau*, 174 U.S.P.Q. 393 (CCPA 1965). Also, the Office must consider the inventions of the cited references in their entireties. Certain individual features from the references may not be chosen and merely lumped together as a mosaic in an attempt to meet the features of the rejected claims. This legal concept is important for the Office to remember when attempting to combine prior art that teach entirely different structures.

Keeping in mind that the Office is not allowed to pick and choose certain elements of Young, such as the amino acid linker, to the exclusion of other elements, applicants submit that if the amino acid linker of Young, which is meant to keep the moiety apart is incorporated into the DeVico '454 or '723 structures then the DeVico '454 or '723 will no longer function as intended. Clearly, the DeVico '454 or '723 structures were generated with the crosslinking agent for the specific reason of maintaining the integrity of complex because as stated numerous times in both DeVico '454 and '723, complexes formed by affinity binding did not provide for integrity of the complex during administration. Clearly, there is no teaching or guidance in either reference for the inclusion of a linker and more important, where the linker is supposedly positioned in the DeVico '454 and '723 structures. Is the amino acid linker added onto one end of DeVico '454 and '723 structures or does it replace the crosslinking agent. Clearly, it cannot

replace the crosslinking agent because then the DeVico '454 and '723 polypeptide structures will not operate as intended if the crosslinking agent is removed.

In the reverse, if the crosslinking agent of DeVico '454 and '723 is introduced into the Young soluble viral receptor-ligand fusion molecule, the question still remains as to the placement of this crosslinking agent. If the amino acid linker is replaced by the crosslinking agent then the component moieties of the viral receptor-ligand fusion molecule may bind to each other instead of the viral receptor moiety binding to the envelope component of the viral vector and the ligand moiety binding to a cell-type specific cellular receptor. Clearly, if this replacement occurs then the Young soluble viral receptor-ligand fusion molecule will become inoperable and not provide for entry of the viral vector into the cell. In light of the fact that all reference will no longer operate as intended, there is no teaching or suggestion to go in the direction of applicants' claimed invention.

Applicants stress that the inclusion of a separation process discussed in the Stratagene Catalog or the C-terminal mutation of Freed, et al. does not remedy the shortcomings of the Young and DeVico '454 or DeVico '723 references.

Applicant points out that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination and suggesting the desirability of the combination. Applicant respectfully submits that the Office's statement that "the claimed invention would be obvious to one having ordinary skill in the art" is not sufficient by itself to establish *prima facie* obviousness. According to the Board in *Ex parte Obukowicz*, 27 U.S.P.Q. 2d 1063, 1065 (B.P.A.I. 1992):

> "In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art....The examiner can satisfy this burden only by showing some **objective** (emphasis added) teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teaching of the references."

See also *Ex parte Humphreys*, 24 U.S.P.Q. 2D 1255, 1262 (B.P.A.I. 1992) where the Board addressed this very issue and determined the Office was wrong in rejecting the claims for obviousness because the examiner's rejection was not **specific** as to how one of ordinary skill in the art would have found it obvious to combine the references. Furthermore, the Board noted the examiner had not explained with any **specificity what areas of the references would suggest the combination.** This is the

circumstance here. The Office has not identified **any objective or specific motivation or suggestion in the cited references that would motivate one skilled in the art to combine the references.** Thus, the Office seems to be merely reinterpreting the prior art in light of applicant's disclosure, in order to reconstruct applicant's claimed invention, but without any instructional or motivating basis in the references themselves. The Office looked at various aspects of the invention, rather than examining the invention as "a whole," found these elements separately in the art, and reassembled them to arrive at something allegedly approximating the present invention. Such approach is improper and legally insufficient to establish a *prima facie* case of obviousness.

In conclusion, the proposed combination does not render applicants' claimed invention *prima facie* obvious because there is no motivation, suggestion or basis in Young and DeVico '454 or DeVico '723 to combine the references and if the teachings of the references were combined then the respective polypeptide structures would no longer function as intended and would be rendered inoperable.

Applicants have cancelled claims 1 and 5-9, amended claims 10-16 to depend from allowable claims 2-4, thereby obviating this rejection.

Judicially Created Doctrine of Obviousness-type Double Patenting

Claims 1, 5-11 and 15-16 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of DeVico '723 or claim 1 of DeVico '454 in view of Young and Freed, et al.

The initial burden of establishing a *prima facie* basis to deny patentability to a claimed invention is always upon the examiner. *In re Oetiker*, 977 F.2d 1443,24 USPQ 1443, (Fed. Cir. 1992). The test for obviousness-type double patenting is whether the claimed invention of the subject application would have been obvious from the subject matter of the **claims** in DeVico '454 or DeVico '723 in view of Young and Freed, et al.. *See In re Longi*, 774 F.2d 1100, 225 USPQ 645 (Fed.Cir. 1985).

As discussed above, applicants' claimed invention is a chimeric polypeptide comprising: a HIV virus coat polypeptide sequence and a viral receptor polypeptide sequence, wherein the HIV virus coat polypeptide sequence has a bonding affinity for the viral receptor polypeptide sequence, wherein the HIV virus coat polypeptide sequence and the viral receptor polypeptide sequence are linked by an amino acid spacer of sufficient length to allow the HIV virus coat polypeptide sequence and the viral receptor polypeptide

sequence to bind to each other. Furthermore, the HIV virus coat polypeptide (gp120) comprises a mutated furin cleavage site on the C-terminus of gp120.

The DeVico '454 and '723 claims describe a virus coat polypeptide sequence and the receptor polypeptide sequence that are covalently bonded to each other. The claims of these references provide no teaching or suggestion to include an amino acid linker between the virus coat polypeptide sequence and the receptor polypeptide sequence. Further the claims of these references provide no teaching or suggestion that the virus coat polypeptide sequence is mutated at a C-terminus furin cleavage.

The claims of the Young reference provide no suggestion or teaching for an amino acid linker and they are completely devoid of any mention of a virus coat polypeptide sequence that is mutated at a C-terminus furin cleavage site. Thus, one reading the claims of DeVico '454 or DeVico '723 in view of the claims of Young would not be motivated to go in the direction of applicants' claimed invention.

Clearly, the question to be asked in whether there is a patentable distinction between the claims of DeVico '454 or DeVico '723 in view of the claims of Young and applicants' claimed invention. Applicants' inclusion of a mutation at a C-terminus furin cleavage site of gp120 is patentably distinct from any reference that teaches a gp120 sequence that does not include this mutation. The complexes claimed in DeVico '454 or DeVico '723 in view of the soluble molecules claimed by Young that are completely devoid of this mutated furin cleavage site do not rendered applicants' claimed invention as obvious. Because the Office has not provided the applicants with any factual basis and/or rationale to support the conclusion that the claimed invention is an obvious variation of DeVico '454 or DeVico '723 in view of Young, the judicially created double patenting rejection cannot stand. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Fees Payable

Applicants have added eleven (11) new dependent claims. However, applicants have cancelled one independent claim and 35 dependent claims, and as such, no fee is due. In the event any fee or charge is properly payable in connection with the entry of this Amendment the United States Patent and Trademark Office is hereby authorized to charge the amount to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

CONCLUSION

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Winkler reconsider the patentability of claims 1-16, in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Winkler is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,

Marianne Fuierer
Reg. No. 39,983
Attorney for Applicants

**INTELLECTUAL PROPERTY/
TECHNOLOGY LAW
Telephone: (919) 419-9350
Fax: (919) 419-9354
Attorney Ref: 4115-144 CIP**